

## Mechanistic Investigations on *N*-Halosulphonamides. Kinetics of Oxidation of Thiocarbonohydrazide in the Free and Metal-bound States and Diethylidene Thiocarbonohydrazide, in Aqueous and Partially Aqueous Media

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The kinetics of oxidation of thiocarbonohydrazide (TCH) in the free and Zn(II)-bound states and its hydrazone, by *N*-chlorobenzenesulphonamide (chloramine-B) in aqueous perchloric acid and by *N,N*-dichlorobenzenesulphonamide (dichloramine-B) in water-methanol (1:1, v/v) in the presence of perchloric acid, have been investigated. Oxidation by both chloramine-B and dichloramine-B shows first-order kinetics in [oxidant] and fractional order in [substrate]. The rates of reactions are independent of  $[H^+]$ . Addition of the reduced product of the oxidant (benzenesulphonamide) or a variation in ionic strength of the reaction medium has no significant effect on the rate of oxidation, in all cases. However, a decrease in the relative permittivity of the medium, effected by changing the solvent composition with methanol, decreases the rate. Both the Michaelis-Menten type and two-pathway mechanisms are discussed in order to explain the observed results. The rate-limiting steps have been identified and the rate coefficients of these steps calculated at different temperatures by varying the substrate concentrations at each temperature. The latter constants have been used to compute the activation parameters from the Arrhenius plots. The metal complexation of thiocarbonohydrazide has little effect either on the rate of oxidation or kinetic order, while conversion to its hydrazone enhances the rate of oxidations with both the oxidants.

The chemistry of S-N donor ligands such as thiosemicarbazide and its homologues and derivatives is of interest due to their synthetic and analytical applications and biological activity.<sup>1-5</sup> They are good metal chelating agents and find applications in the characterisation of several organic compounds. They are potential pesticides and fungicides and are active against influenza, protozoa, smallpox, and certain kinds of tumour.

Thiocarbonohydrazide ( $H_2NHNCSNHNH_2$ ) is a member of the structural sequence thiourea, thiosemicarbazide, and thiocarbonohydrazide and has close links with thiocarbamic and thiocarbazoic acids as well as with aminoguanidines.<sup>2</sup> The chemical behaviour of thiocarbonohydrazide is similar to its keto-analogue carbohydrazide. Thiocarbonohydrazides possess anticarcinogenic and antibacterial properties. The parent compound exhibits a toxicity towards the housefly comparable to that of DDT. It also shows fungicidal properties and has been tested against different species. Although it has been extensively used as a metal chelating agent,<sup>1-3</sup> there are no reports on the mechanistic aspects of its reactions in solution. As a part of our mechanistic investigations on reactions of biologically active substrates in the liquid phase, we now report the kinetics of oxidation of thiocarbonohydrazide in the free and metal-bound states and its hydrazone, by *N*-chlorobenzenesulphonamide (chloramine-B) in aqueous perchloric acid and by *N,N*-dichlorobenzenesulphonamide in water-methanol (1:1, v/v) in the presence of perchloric acid.

### Experimental

**Materials and Methods.**—Chloramine-B (CAB, sodium *N*-chlorobenzenesulphonamide) was prepared by the partial chlorination of benzenesulphonamide in aq. NaOH (4 mol

$dm^{-3}$ ).<sup>6</sup> Dichloramine-B (DCB, *N,N*-dichlorobenzenesulphonamide) was obtained by the chlorination of chloramine-B<sup>7</sup> in aqueous solution. The purity of the oxidants was checked by i.r. spectroscopy and estimation of the amount of active chlorine present. Stock solutions (*ca.* 0.05 mol  $dm^{-3}$ ) of chloramine-B in doubly distilled water and dichloramine-B in methanol were prepared, standardised, and stored in dark-coloured bottles.

Thiocarbonohydrazide was prepared by refluxing a mixture of carbon disulphide and hydrazine hydrate at 90 °C for 1 h. The colourless crystals which separated out were recrystallised from water (m.p. 168 °C, decomp.). Thiocarbonohydrazide was characterized by i.r. spectroscopy and sulphur estimation. The complex bis(thiocarbonohydrazide) zinc(II) chloride was obtained by mixing warm solutions of zinc chloride in dimethylformamide (DMF)-water (5:1, v/v) and thiocarbonohydrazide in DMF, in a *ca.* 1:2 mole ratio. The colourless crystals of the metal complex separated out when the solution was allowed to stand for > 1 h, and were filtered and washed with hydrochloric acid (0.1 mol  $dm^{-3}$ ) and then dried *in vacuo* over  $P_2O_5$ .

The hydrazone diethylidene thiocarbonohydrazide was prepared<sup>8</sup> by adding a 50% excess of acetaldehyde in ethanol to a solution of thiocarbonohydrazide in acetic acid (1 mol  $dm^{-3}$ ) and refluxing the resulting mixture for 1 h. The pale yellow crystals obtained were recrystallised from DMF (m.p. 245 °C). The hydrazone was further characterised by i.r. spectroscopy and sulphur estimation.

The stock solutions (*ca.* 0.05 mol  $dm^{-3}$ ) of thiocarbonohydrazide, its metal complex, and hydrazone were prepared in aqueous perchloric acid (0.1 mol  $dm^{-3}$ ) because their aqueous solutions were unstable and decomposed when left to stand. In aqueous perchloric acid the solutions were stable for several days. The ionic strength of the medium was



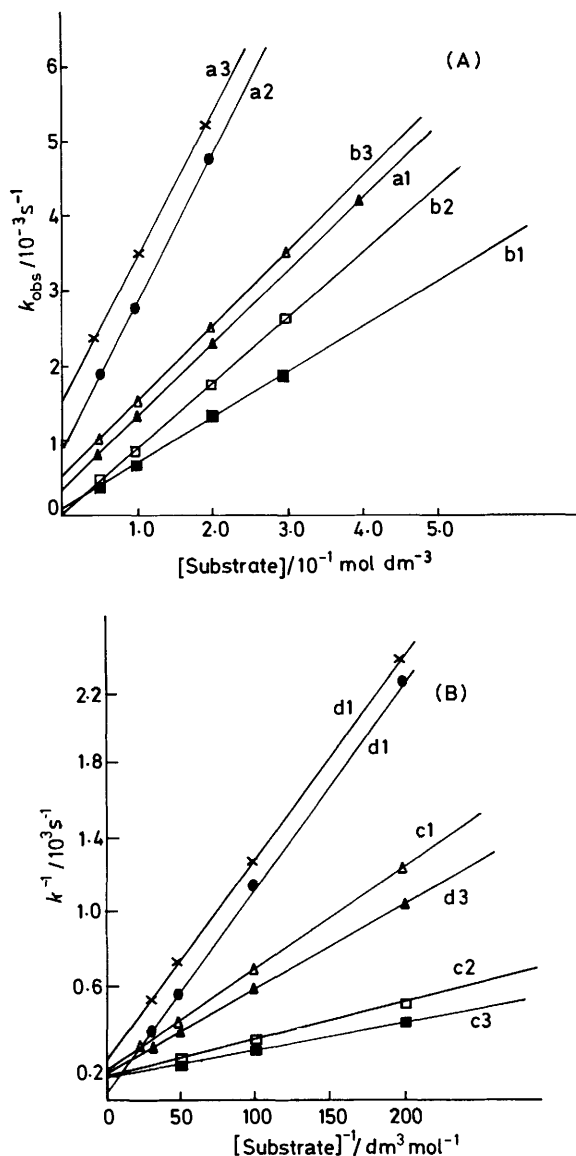


Figure. (A) Plots of  $k_{\text{obs}}$  versus [substrate]; a, CAB; b, DCB; 1, TCH; 2, Complex; 3, hydrazone. (B) Plots of  $1/k_{\text{obs}}$  versus  $1/[\text{substrate}]$ ; c, CAB; d, DCB; 1, TCH; 2, Complex; 3, hydrazone.  $10^3[\text{oxidant}]_0 = 20[\text{HClO}_4] = 1.0\text{mol dm}^{-3}$ ,  $I = 0.3\text{mol dm}^{-3}$ ,  $T = 293\text{K}$ .

The rates were unaffected by a variation of  $[\text{HClO}_4]$  at constant  $[\text{oxidant}]$  and  $[\text{substrate}]$ , in all cases. Addition of the reduced product of the oxidant (benzenesulphonamide) or a variation in the ionic strength of the medium had no significant effect on the rate of oxidation for all the substrates. A decrease in relative permittivity ( $\epsilon_r$ ) of the medium, effected by changing the solvent composition with methanol, decreased the rate of all oxidations.

The substrate concentration was varied at different temperatures and the coefficients of the rate-controlling steps were evaluated as described earlier. These constants were used to calculate the activation parameters from the Arrhenius plot (Table 3).

### Discussion

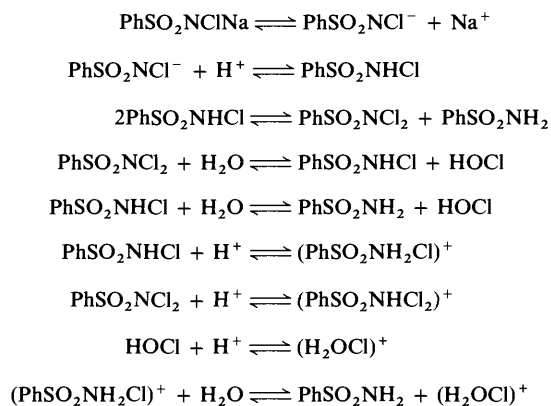
Chloramine-B ( $\text{PhSO}_2\text{NClNa}$ ) and dichloramine-B ( $\text{PhSO}_2\text{NCl}_2$ ), like chloramine-T, dichloramine-T, and bromamine-B, furnish different reactive species in aqueous or partially aqueous solutions depending upon the pH of the medium.<sup>13-18</sup> The

Table 2. Kinetic and thermodynamic parameters for oxidations of thiocarbonohydrazide and its metal complex and hydrazone, by chloramine-B (CAB) in aqueous perchloric acid and dichloramine-B in water-methanol (1:1, v/v).

Observed order	TCH	Zn(TCH) <sub>2</sub> Cl <sub>2</sub>	Hydrazone			
[CAB]	1.0	1.0	1.0			
[TCH]	0.8	0.6	0.5			
[H <sup>+</sup> ]	0	0	0			
[DCB]	1.0	1.0	1.0			
[TCH]	0.8	0.8	0.7			
[H <sup>+</sup> ]	0	0	0			
Parameters	Set I <sup>a</sup>	Set II <sup>b</sup>	Set I <sup>a</sup>	Set II <sup>b</sup>	Set I <sup>a</sup>	Set II <sup>b</sup>
Chloramine-B oxidations						
$E_a/\text{kJ mol}^{-1}$	122.2	83.3	61.5	38.3	38.3	37.4
$\log A$	19.7	12.8	8.92	5.02	4.79	4.94
$\Delta H^\ddagger/\text{kJ mol}^{-1}$	103.0	80.4	54.7	36.7	34.9	34.04
$\Delta S^\ddagger/\text{J K mol}^{-1}$	68.6	-10.5	-97.6	-152.5	-144.0	-161.0
$\Delta G^\ddagger/\text{kJ mol}^{-1}$	82.9	83.4	83.3	81.4	83.1	81.2
Dichloramine-B oxidations						
$E_a/\text{kJ mol}^{-1}$	27.18	34.6	23.9	58.2	34.3	49.2
$\log A$	7.06	3.95	2.2	8.31	3.92	6.74
$\Delta H^\ddagger/\text{kJ mol}^{-1}$	24.12	34.75	20.08	57.4	32.35	41.2
$\Delta S^\ddagger/\text{J K mol}^{-1}$	-207.9	-169.19	-190.80	-87.9	-175.55	-142.2
$\Delta G^\ddagger/\text{kJ mol}^{-1}$	85.04	84.32	84.50	83.2	83.78	82.9

<sup>a</sup> Calculated using  $k_2$  values at different temperatures; see equation (3) and text. <sup>b</sup> Calculated using  $k_3$  values at different temperatures; see equation (6) and text.

following equilibria exist in the aqueous or partially aqueous solutions of chloramine-B and dichloramine-B (Scheme 2).



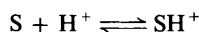
Scheme 2.

Therefore, the probable reactive species in aqueous acid or partially aqueous solutions of chloramine-B and dichloramine-B are  $\text{PhSO}_2\text{NHCl}$ ,  $\text{PhSO}_2\text{NCl}_2$ , and  $\text{HOCl}$  at low  $[\text{HClO}_4]$  and  $(\text{PhSO}_2\text{NH}_2\text{Cl})^+$ ,  $(\text{PhSO}_2\text{NHCl}_2)^+$ , and  $(\text{H}_2\text{OCl})^+$  at high  $[\text{HClO}_4]$ .

**Table 3.** Calculated equilibrium constants and rate coefficients of the rate-determining steps at different temperatures for the oxidations of thiocarbonohydrazide and its metal complex and hydrazone, by chloramine-B in aqueous perchloric acid and dichloramine-B in water-methanol (1:1, v/v).

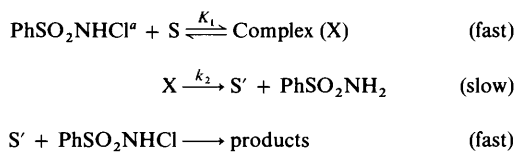
T/K	Chloramine-B oxidations			Dichloramine-B oxidation		
	$K_1/\text{dm}^3 \text{ mol}^{-1}$	$k_2/10^{-3} \text{ s}^{-1}$	$k_3/10^{-2} \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$	$K_1/\text{dm}^3 \text{ mol}^{-1}$	$k_2/10^{-3} \text{ s}^{-1}$	$k_3/10^{-2} \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$
<b>Thiocarbonohydrazide</b>						
283	52.5	2.4	2.7	19.4	2.8	3.4
288	30.7	4.5	4.7	15.4	3.2	4.6
293	26.9	6.3	8.8	16.7	4.1	4.8
298	10.6	—	15.6	23.3	5.0	7.7
<b>Metal complex</b>						
288	34.2	6.3	12.5	9.1	7.1	6.0
293	30.1	8.3	18.3	11.4	8.3	9.2
298	22.1	14.2	21.8	14.9	10.0	14.7
<b>Hydrazone</b>						
288	30.1	7.1	14.7	32.9	5.09	7.4
293	41.3	8.3	20.0	35.2	6.3	10.8
298	38.6	12.5	26.0	41.5	8.4	14.0

In solutions of the substrate (S) in acid the following protonation equilibrium also exists.



Under strongly acidic conditions most of the substrate exists in the protonated form.

**Mechanism of Oxidations.**—The kinetic results (first order in [oxidant], fractional order in [substrate], and zero order in  $[\text{H}^+]$ ) together with the lack of influence on the rate of oxidation of either added benzenesulphonamide or increase in ionic strength may be explained by either a Michaelis–Menten type mechanism (Scheme 3) or a two-pathway mechanism (Scheme 4).



**Scheme 3.** <sup>a</sup> Similarly for  $\text{PhSO}_2\text{NCl}_2$ .

Based on Scheme 3 the following rate laws were deduced.

$$-\frac{d[\text{oxidant}]}{dt} = \frac{K_1 k_2 [\text{oxidant}][\text{S}]}{1 + K_1[\text{S}]} \quad (1)$$

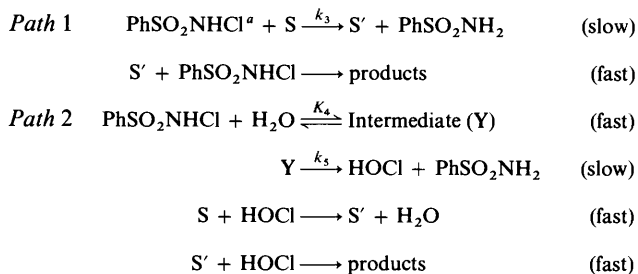
$$\text{i.e.} \quad k_{\text{obs}} = \frac{K_1 k_2 [\text{S}]}{1 + K_1[\text{S}]} \quad (2)$$

$$\text{or} \quad \frac{1}{k_{\text{obs}}} = \frac{1}{K_1 k_2 [\text{S}]} + \frac{1}{k_2} \quad (3)$$

The plots of  $1/k_{\text{obs}}$  versus  $1/[\text{S}]$  were reasonably linear in all cases in accordance with equation (3). From the slopes and intercepts of the plots, the constants  $k_2$  and  $K_1$  were calculated. Further, the substrate concentration was varied at different temperatures (283–298 K) and the constants  $k_2$  and  $K_1$  were computed at each temperature (Table 2). The values of  $k_2$  were

used to calculate the activation parameters from the Arrhenius plots.

The two-pathway mechanism and the related rate laws are as follows:



**Scheme 4.** <sup>a</sup> Similarly for  $\text{PhSONCl}_2$ .

The combined rate law [equation (4)] is in accordance with Scheme 3.

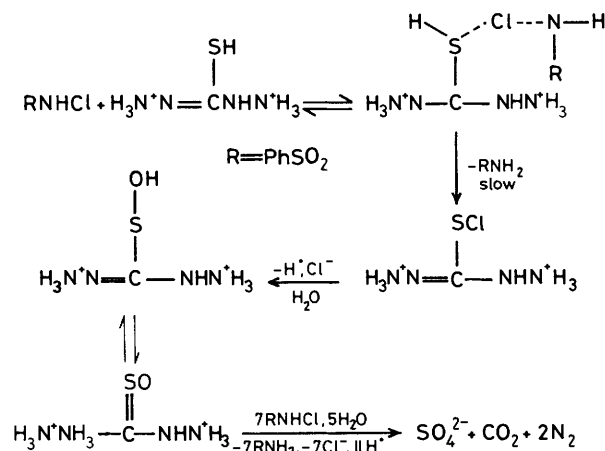
$$-\frac{d[\text{oxidant}]}{dt} = k_3[\text{oxidant}][\text{S}] + \frac{K_4 k_5 [\text{oxidant}][\text{H}_2\text{O}]}{1 + K_4[\text{H}_2\text{O}]} \quad (4)$$

$$\text{i.e.} \quad k_{\text{obs}} = k_3[\text{S}] + \frac{K_4 k_5 [\text{H}_2\text{O}]}{1 + K_4[\text{H}_2\text{O}]} \quad (5)$$

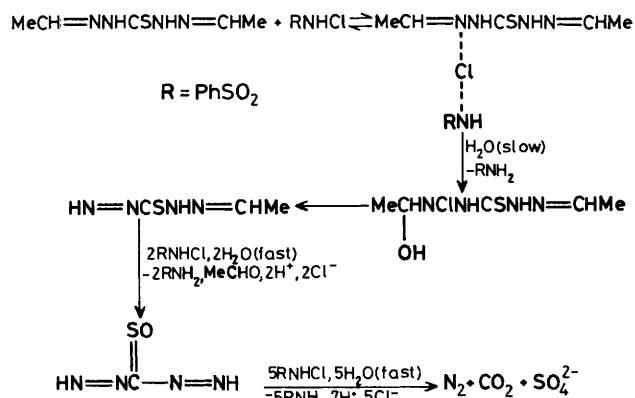
$$\text{or} \quad k_{\text{obs}} = k_3[\text{S}] + k'_5, \text{ where } k'_5 = \frac{K_4 k_5 [\text{H}_2\text{O}]}{1 + K_4[\text{H}_2\text{O}]} \quad (6)$$

The plots of  $k_{\text{obs}}$  versus  $[\text{S}]$  were also linear for all substrates with both oxidants (Figure). The slopes gave  $k_3$  (Table 3). The values of  $k_3$  were calculated at different temperatures (283–298 K) by varying the substrate concentration at each temperature (Table 3). The latter constants were also used to calculate the activation parameters from the Arrhenius plots (Table 2).

Although both the Michaelis–Menten type (Scheme 3) and the two-pathway mechanism (Scheme 4) explain the observed results for the oxidation of thiocarbonohydrazide in the free and metal-bound states and in its hydrazone, by either chloramine-B or dichloramine-B, the latter seems to be preferred, since the direct plots give relatively better correlations (Figure).



**Scheme 5.**



Scheme 6.

Detailed mechanisms of the oxidation of thiocarbonylhydrazide and its hydrazones by  $\text{PhSO}_2\text{NHCl}$  are shown in Schemes 5 and 6; the mechanisms of oxidations by  $\text{PhSO}_2\text{NCl}_2$  and  $\text{HOCl}$  are similar.

The effects of solvent composition on the rates of ion-ion, ion-dipolar molecule, and dipolar molecule-dipolar molecule reactions have been discussed by several authors.<sup>19-22</sup> For the limiting case of zero angle of approach between two dipoles or an ion-dipole system, Amis<sup>19</sup> has shown that a plot of  $\log k_{\text{obs}}$  versus  $1/\epsilon_r$  gives a straight line with a negative slope for the reaction between a negative ion and a dipolar molecule or between two dipolar molecules. The present experimental observations *i.e.* decrease of rate with decrease in relative permittivity\* ( $\epsilon_r$ ) of the medium (by increasing the methanol composition of the medium, 0-40%, v/v in chloramine-B oxidations and 30-60%, v/v in dichloramine-B oxidations) are in agreement with dipolar molecule-dipolar molecule interactions and the reaction pathways proposed to account for the observed kinetic data. The plots of  $\log k_{\text{obs}}$  versus  $1/\epsilon_r$  or % methanol were also linear with negative slopes, for all the oxidations.

The constancy of the free energies of activation gives an indication of the operation of a similar mechanism in all cases. The formation of more ordered activated complexes is evident from the large negative values (with one or two exceptions) of the entropy of activation (Table 2).

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\* Formerly known as dielectric constant.